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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/549,601	08/08/2006	Hiroshi Takaku	2352.008	2223

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EXAMINER	
CHONG, KIMBERLY	
ART UNIT	PAPER NUMBER
1635	
MAIL DATE	DELIVERY MODE
07/10/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/549,601	TAKAKU ET AL.	
	Examiner	Art Unit	
	Kimberly Chong	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 February 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6 and 9-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 9-15* is/are rejected.

7)☒ Claim(s) *5,12,13* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application/Amendment/Claims

Applicant's response filed 02/04/2008 has been considered. Rejections and/or objections not reiterated from the previous office action mailed 10/03/2007 are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

With entry of the amendment filed on 02/04/2008, claims 1-6 and 9-15 are pending and currently under examination in the application.

New Claim Objection and Rejections

Claim Objections

Claims 5, 12 and 13 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claims 5, 12 and 14 recite an HIV agent comprising the oligonucleotide of claims 1 and 2 and fails to further limit claims 1 and 2 which recites an oligonucleotide.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 6, 14 and 15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the claimed composition comprising an oligonucleotide for treatment of HIV, does not reasonably provide enablement for the full scope of a composition which requires *prevention* of HIV. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The instant claims are drawn to a composition comprising an oligonucleotide for the *prevention* of HIV. The *in vivo* inhibition and treatment effects described in the specification at page 10 involve prophetic examples only and have not been reduced to practice. Furthermore, there is no guidance in the specification as filed that teaches how to prevent HIV. Although the specification discloses anti-HIV activity using an antisense oligonucleotide targeted to viral genes, such a disclosure would not be considered enabling since the state of therapeutic antisense-mediated gene inhibition for prevention of disease is highly unpredictable.

The following factors have been considered in the analysis of enablement: (1) the breadth of the claims, (2) the nature of the invention, (3) the state of the prior art, (4) the level of one of ordinary skill, (5) the level of predictability in the art, (6) the amount of direction provided by the inventor, (7) the existence of working examples, (8) the

quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The references cited herein illustrate the state of the art for therapeutic applications using antisense compounds for prevention of viral infections such as HIV: post-filing art such as Lu et al. (Journal of Virology 2004, 7079-7088) outlines the antisense mediated effects of inhibition of HIV and states that antisense targeting of HIV transcripts have been previously reported and the feasibility of such therapy have been established but the data from these studies "have not led to efficacy in the clinic due to low transduction efficiencies and persistence of modified cells."

Stankov (Medical Hypothesis 2000, Vol.54(3):501-502) states that '[t]he aim of antisense antiviral agents is to block …foreign information in a specific and selective way… [and] the optimal theoretical possibility of blocking foreign genetic information is to perform a complete block" (see page 501 paragraph 1). However, Stankov notes that because "[a]ntisense oligos … apparently comprise only a small part of a viral genome…[and] a simple deletion of a relatively short target sequence might well become a mechanism of resistance to antisense oligos …[which] leave viruses a fair chance to survive" (see page 501, paragraph 1).

As outlined above, it is well known that there is a high level of unpredictability in the antisense art for therapeutic prevention of viral disease, such as HIV. The scope of the claims in view of the specification as filed together do not reconcile the unpredictability in the art to enable one of skill in the art to make and/or use the claimed invention.

In view of the unpredictability in the art of antisense-based therapy as outlined above, the specification as filed does not provide adequate guidance that would show how one skilled in the art would practice the claimed invention without undue experimentation. Without further guidance, one of skill in the art would have to practice a substantial amount of trial and error experimentation, an amount considered undue and not routine, to practice the instantly claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 2, 4-6 and 10-15 are rejected under 35 U.S.C. 102(b) as being anticipated by McArthur et al. (U.S. Patent No. 6,808,905).

Claims 1, 2, 4-6 and 10-15 are drawn to an oligonucleotide consisting of a nucleotide sequence that is complementary or an oligonucleotide comprising a nucleotide sequence which specifically hybridizes to a nucleotide sequence consisting of at least 15 successive nucleotides of SEQ ID No. 1 in the range of nucleotides 6 to 44.

McArthur et al. teach an oligonucleotide sequence consisting of a nucleotide sequence that is complementary to at least 15 nucleotides of SEQ ID No. 1 in the range of nucleotides 6 to 44 (see attached sequence alignment). McArthur et al. teach a composition comprising the oligonucleotide and DNA hydration buffer. A pharmaceutically acceptable carrier or diluent is not defined in the specification and therefore for prior art purposes a diluent is any reagent suitable for administration of an oligonucleotide to a cell, such as a buffer. The instant specification discloses on page 6 that specific hybridization of an oligonucleotide encompasses an oligonucleotide that hybridizes with at least 15 nucleotides of SEQ ID No. 1. Therefore, for prior art purposes, "specifically hybridizes" is interpreted to mean an oligonucleotide that is complementary to at least 15 nucleotides of the instantly claimed sequence.

McArthur et al. does not specifically disclose the oligonucleotide specifically hybridizes to a nucleotide sequence consisting of 15 nucleotides of SEQ ID No. 1 nor teach the oligonucleotide is an antisense or an anti-HIV agent however the oligonucleotide taught by McArthur et al. meets all the structural limitations of the instant claims and therefore would then be considered to be an antisense oligonucleotide (an oligonucleotide that binds to a complementary strand) and an anti-HIV agent, absent evidence to the contrary. See, for example, MPEP 2112, which states "…the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable.…Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either

anticipation or obviousness has been established. *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990)."

Thus, the instant claims are anticipated by McArthur et al.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 2, 3 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over McArthur et al. (U.S. Patent No. 6,808,905) in view of Nikiforov et al. (PCR Methods and Applications, 1994, Vol. 3: 285-291).

Claims 1, 2, 4-6 and 10-15 are drawn to an oligonucleotide consisting of a nucleotide sequence that is complementary or an oligonucleotide comprising a nucleotide sequence which specifically hybridizes to a nucleotide sequence consisting of at least 15 successive nucleotides of SEQ ID No. 1 in the range of nucleotides 6 to 44, wherein at least one internucleotide bond is a phosphorothioate bond.

McArthur et al. is relied upon as above. McArthur et al. do not teach modification of oligonucleotide primers with phosphorothioate bonds (see pages 287-288).

Nikiforov et al. teach modification of the oligonucleotide with phosphorothioate bonds protects the oligonucleotide from enzymatic degradation.

A person of ordinary skill in the art, upon reading Nikiforov et al., would have recognized the desirability of improved nuclease resistance of oligonucleotides comprising phosphorothioate bonds. Furthermore, the incorporation of phosphorothioate bonds would have reasonably been expected to be applicable to the claimed oligonucleotide, thus it would have been obvious to a person of ordinary skill in the art to try the modifications taught by Nikiforov et al. in an attempt to impart improved nuclease resistance to oligonucleotides.

Thus in the absence of evidence to the contrary, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Response to Applicants Arguments

Re: Priority

Receipt is acknowledged of translation of foreign priority documents 2003-076254 filed 02/04/2005.

Re: Sequence Compliance

Receipt is acknowledged of amendment to the specification to include the appropriate sequence identifiers in the brief description of the drawings and also submission of a substitute sequence listing filed 02/04/2008. .

Re: Claim Rejections - 35 USC § 112

The rejection of claims 4, 6, 10, 11, 14 and 15 under 35 U.S.C. 112, first paragraph is withdrawn in response to claim amendments.

Re: Claim Rejections - 35 USC § 102

The rejection of claims 1 and 2 under 35 U.S.C. 102(b) as being anticipated by Schubert et al. (U.S. Patent No. 5,847,096) is withdrawn in response to Applicant's arguments.

Re: Claim Rejections - 35 USC § 102 or 35 USC § 103

The rejection of claims 5 and 12 under 35 U.S.C. 102(b) or 35 U.S.C. 103(a) as being anticipated by or obvious over Schubert et al. (U.S. Patent No. 5,847,096) is withdrawn in response to Applicant's arguments.

Re: Claim Rejections - 35 USC § 103

The rejection of claims 1-6 and 9-15 under 35 U.S.C. 103(a) as being unpatentable over Mourich et al. (US 2005/0222068) in view of Galderisi et al. (J. Cellular Physiology 1999, Vol. 181: 251-257) is withdrawn as Mourich et al. is not available as prior art.

Sequence Alignments

RESULT 2
US-10-145-289-2/c
; Sequence 2, Application US/10145289
; Patent No. 6808905
; GENERAL INFORMATION:
; APPLICANT: James G. McArthur
; APPLICANT: Dale John Talbot

; APPLICANT: Andrew D. Simmons
; APPLICANT: Ryan McGuinness
; APPLICANT: Michael Kelly
; APPLICANT: Lisa V. Tsui
; APPLICANT: Thomas Dull
; TITLE OF INVENTION: LENTIVIRAL VECTORS ENCODING CLOTTING
; TITLE OF INVENTION: FACTORS FOR GENE THERAPY
; FILE REFERENCE: 131.2USU1
; CURRENT APPLICATION NUMBER: US/10/145,289
; CURRENT FILING DATE: 2002-05-14
; PRIOR APPLICATION NUMBER: 60/291,083
; PRIOR FILING DATE: 2001-05-14
; NUMBER OF SEQ ID NOS: 10
; SOFTWARE: FastSEQ for Windows Version 4.0
; SEQ ID NO 2
; LENGTH: 15
; TYPE: DNA
; ORGANISM: Artificial Sequence
; FEATURE:
; OTHER INFORMATION: primer
US-10-145-289-2

Query Match 38.5%; Score 15; DB 3; Length 15;
Score over Length 100.0%;
Best Local Similarity 93.3%; Pred. No. 1.1e+04;
Matches 14; Conservative 1; Mismatches 0; Indels 0; Gaps 0;

Qy 13 CUGAAGCGCGCACGG 27
|:||||||||||||
Db 15 CTGAAGCGCGCACGG 1

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly Chong whose telephone number is 571-272-3111. The examiner can normally be reached Monday thru Friday between 7-4 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached at 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

/Kimberly Chong/
Examiner
Art Unit 1635